choice for young patients (pts) with severe manifestations of the disease. In this study, we analyze the results in 19 boys transplanted in 2 BMT centers between 04/92–03/05. Age: 7 months to 14 years (M: 2 years). All but one pt had the classical syndrome with many serious infections (especially CMV related) or autoimmunity prior to transplant.Stem cell source: Bone marrow from related: 9 pts or cord blood (CB) from unrelated donors:10 pts. HLA disparities: Bone marrow: 6/6: 7 pts and 5/6: 2 pts; CB: 6/6: 1 pt, 5/6: 6 pts and 4/6: 3 pts. Preparatory regimen: Busulfan(BU) + Cyclophosphamide(CY) ± ATG: 17 pts; BU + Fludara: 1 pt, and BU + CY + Thiotepa: 1 pt. GVHD prophylaxis:cyclosporine (csa) + methotrexate: 8 pts; csa + steroids: 10 pts, and csa + MMF: 1 pt. ATG was added to pts receiving transplants from donors other than HLA identical siblings. TNC infused: bone marrow 2, 3—10 × 10*8/kg (M: 3, 08) and CB: 4, 9*mdash;8,8–10*7/kg (6, 12). Sixteen pts (84%) are alive between 117 to 3997 days (M: 776 days) after SCT. All pts survived more than 28 days and were evaluable for engraftment. Mucositis grade I-II occurred in most pts. VOD (mild): 2 pts. Three pts died on day +34 (Unrelated CB 4/6, pulmonary aspergilosis), day +65, and day +117 (HLA identical siblings*mdash;CMV pneumonitis). Primary graft failure occurred in 2 pts who received Unrelated 4/6 CB and only 1 pt is alive and well on day +370 after the second CB infusion. This pt developed acute (grade III) and chronic (extensive) GVHD and many other severe viral infections. Seventeen pts engrafted and the median time to reach ANC > 500/ul was 22 days (10–30) and platelets > 20.000/ul was 35 days (14–77). Acute GVHD occurred in 7/17 pts (only one pt grade IV) and chronic GVHD in 3/16 pts (extensive and severe). Three pts are still receiving treatment with immunosupressive drugs. Full donor chimerism was achieved in 15/16 surviving pts.Viral infections were frequent complications, especially in the URD cord blood transplants.We conclude that SCT in pts with WAS has an excellent survival and should be indicated to young pts with severe manifestations of the disease.

367

EARLY HEPATIC COMPLICATION IN FIRST YEAR AFTER BONE MARROW TRANSPLANTATION IN MAJOR βTHALASSEMIA PATIENTS

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Liver complications are one of the major causes of morbidity and mortality following BMT. Determination of the factors of liver injury leads to earlier diagnosis after BMT and improves prognosis. We studied 113 major βthalassemic patients who have been transplanted from 1990–2000 in bone marrow transplantation center of Shariati Hospital. Sixty-two were male and 51 were female. Twenty-seven patients were class 1, 56 were class 2, and 30 were class 3. The median age of each class were 6.5, 6.3, and 8.7 year. Conditioning regimen consisted of busulfan (3.5–4 mg/Kg) and cyclophophamide (40–50 mg/Kg).For GVHD prophylaxis we gave cyclosporine ± metothoroxate. Grade of liver fibrosis was defined by biopsy in all patients before BMT. All patients and their donors tested for HBSAg, HBSAb, HCVAb, and CMVAb with RIA method. We assessed causes of liver dysfunction before and after transplantation and effect of high ferritin level on liver function. Hepatic dysfunction in first year after transplantation was seen in 86 (76%) patients. Causes of liver dysfunction consisted of 53.1% GVHD, 15.93% cyclosporine hepatotoxicity, 7.07% conditioning regimen hepatotoxicity, and VOD. In all three classes hepatic GVHD, cyclosporine toxicity, death, and normal liver function post BMT had significant relation with hepatic dysfunction before BMT ($P = .001$). In patients with ferritin level more than 1000, there was significant hepatotoxicity with conditioning regimen ($P = .001$). According to our study, hepatic GVHD (%53.1) is the most common cause of hepatic dysfunction in all three classes.

368

BOOSTING OF THYMIC T LYMPHOCYTE MATURATION AND EXPORT BY INFUSION OF T CELL DEPLETED DONOR PERIPHERAL BLOOD STEM CELLS TO A SCID PATIENT WITH DECLINING T LYMPHOCYTE COUNTS AFTER HLA MISMATCH ALLOGENEIC BMT

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The patient was born June 1971. The diagnosis of SCID was established at 3 months of age. Retrospective analysis revealed JAK3 mutations compatible with autosomal recessive SCID. In December 1971, he was treated with 3 infusions of BM aspirates, totaling 7×10^7 nucleated cells from his mother's brother, selected because of a negative donor versus recipient MLR. Retrospective HLA-typing revealed DRB1 and DQB1 identity but multiple class I mismatches. No conditioning or GvHD prophylaxis was given. A skin rash was observed 2 weeks after the first infusion. No other signs of GvHD occurred. The lymphocyte count was 5100 per mL one year after transplantation, ca. 50% of the PBMC expressed the not shared donor derived HLA class I antigens and 63% were SRBC rosetting cells. Mitogen responses were normalized but there was persistent absence of donor derived Rh(D) positive red blood cells and of IgG and IgA production, whereas IgM isoagglutinin developed normally. Low blood T lymphocyte count was noted in 1988. In 2000, the blood CD4+ count was decreased to 200 per mL, and the CD8+ count to 300 per mL. The TRECs containing CD4+ cell count was 0.02 per mL and the TRECs containing CD8+ cell count 0.03 per mL (1 to 2% of normal for age). Bone marrow CD34+ cells, peripheral blood neutrophils, and B lymphocytes were of recipient origin, whereas the few circulating T lymphocytes were of donor origin (microsatellite analysis). A peripheral blood stem cell harvest was procured (December 2001) from the original donor and CD34+ purified using the CliniMACS device and the CliniMACS CD34 reagent set. The patient received a total of 2.7×10^6 CD34+ cells and 0.08×10^4 CD3+ cells per kg BW. Cyclosporin was given for 3 month as GvHD prophylaxis. No evidence of GvHD occurred. Subsequent blood tests have shown no major change in the number of circulating CD3+, CD4 + CD45RA, or CD8 + CD45RA lymphocytes over time. However, the number of CD4 and CD8 cells containing TRECs increased within the 600 days after boosting to 1.5 and 2.5 per mL, respectively, (normal for recipient age). A subsequent decline has been observed. We conclude that descendants from the boosting donor CD34+ cells were able to undergo maturation in the thymus but a persistent take of donor derived CD34+ cells was not established.

369

BUSULFEX®, CYCLOPHOSPHAMIDE, THYMOGLOBULIN® (BU/CY/Thymo) AS PREPARATIVE REGIMEN FOR ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) IN CHILDREN WITH NON-MALIGNANT DISORDERS (NMD)

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Background: Graft failure and GVHD remain major causes of failure in HSCT for children with non-malignant disorders (MND). Oral busulfan (BU), cyclophosphamide (CY), equine antithymocyte globulin (ATG) is a standard preparative used for children with NMD. We present preliminary data for a preparative regimen of Bulsufex®, cyclophosphamide, and Thymoglobulin® (BU/CY/Thymo). The regimen was developed for ease of administrtion, especially for young children, and theorectic reduction of GVHD secondary to more in vivo T cell depletion associated with Thymoglobulin® compared to equine ATG. **Methods:** The regimen included Busulfex® [0.8 mg/kg (>12 kg) or 1.1 mg/kg (≤12 kg)] q6 hour × 16 (dose adjusted to target AUC = 1125 μM-minute). Cyclophosphamide (50 mg/kg/day × 4), Thymoglobulin® (2.5 mg/kg/day × 4) with CSA and short course MTX (or methylpredisone for

cord blood). **Results:** 13 patients have been enrolled: LCH (3), HLH (2), Wiscott-Aldrich (1), mannosidosis (2), Krabbe's (1), sickle cell (1), thalassemia (2), and Kostmann's (1). Median age = 2.2 yearrs (0.4–9.1). Stem cell sources were: MSD (3), unrelated UCB (3–5/6 HLA matched, 1–6/6 HLA matched), 6/6 unrelated marrow (5), 6/6 unrelated PBSC (1). Thymoglobulin®toxicities were: (1) seizure course completed and (1) grade IV hypotension (course aborted after two doses). No other non-hematologic grades 3–4 toxicities were observed. All patients achieved >90% stable donor chimerism with no primary or secondary graft failure. Median ANC recovery = 15 days (11–35). Three patients died of infections before day 100. One pateint developed acute GVHD (grade 2 skin only) and limited chronic GVHD (the patient with aborted Thymoglobulin® course). Ten (77%) survived with median follow-up of 410 days (90–1030). **Conclusions:** This preparative regimen is very well tolerated with to date no graft failure and stable donor chimerism even with cord blood. Thymoglobulin®appears to provide good in vitro T-cell depletion with minimal GVHD. Additional patients need to be enrolled to verify these results.

370

COMBINED HOME ENZYME REPLACEMENT THERAPY AND UNRELATED CORD BLOOD TRANSPLANT FOR HURLER'S SYNDROME (MPSI)

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Hurler's syndrome is caused by mutations in the αiduronidase gene and results in progressive deterioration of the central nervous system. Allogeneic bone marrow transplantation before the age of 2 years halts disease progression and prolongs life. Enzyme replacement therapy (ERT) reduces lysosomal storage of mucopolysaccharides in the liver and ameliorates extracranial manifestations of disease. In most instances, ERT occurs in a day hospital setting. Since enzyme replacement therapy can mitigate airway and pulmonary manifestation of MPS I, we hypothesized that ERT in the peri-transplant period (pre-HSCT and immediately post-HSCT) would decrease transplant related complications. We performed combined ERT and HSCT in a 12 month old boy with MPSI. The patient received his first dose of Aldurazyme at 5 months of age, shortly after MPSI diagnosis. He had received 16 infusions prior to referral to our center. Throughout his pre-transplant workup, the patient received ERT at the local Transplant House by a visiting nurse. There were no infusion related toxicities. The patient received a 5/6 unrelated cord blood unit and engrafted on day +12. Hyperacute GVHD was treated successfully with high dose methylprednisolone pulse. Following engraftment, the child received 8 additional doses of Aldurazyme. One year following transplant, he continues to have normal urine GAGs, normal enzyme level, and continues to have developmental improvements. We conclude that in this case of combined outpatient ERT infusion with HSCT, pre- and post-transplant ERT does not interfere with engraftment or developmental improvements.

371

BONE MARROW TRANSPLANTATION IN A CHILD WITH TYPE C OF NIEMANN-PICK DISEASE (SECOND CASE IN THE WORLD)

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Niemann-Pick Disease Type C (NPC) is a lysosomal storage disease caused by an error in cellular trafficking of exogenous cholesterol resulting in accumulation of unesterified cholesterol. Hematopoietic stem cell transplantation for Niemann-Pick disease is considered experimental, investigational, and unproven. We report a 4-years 7 and months old girl with Niemann-Pick type C disease who received an allogeneic BMT. Her disease presented with prolonged neonatal icter, hepatosplenomegaly, failure to thrive, and progressive neurodevelopmental delay from 2 years ago. Bone marrow biopsy revealed abundant lipid-filled foamy macrophages. Her serum sphingomyelinase assey was normal. She received hematopoietic stem cells from a healthy HLA-identical female sibling, 19 year old, donor. She had neutrophil recovery (WBC0.5$\times$ 10^9/L) at day 17 and platelet recovery (platelet $> 20 \times 10^9$/L) at day 33 after transplantation. She had grade 1 skin GVHD. She had no serious infection or complication and was discharged after 38 days. Full engraftment was evidenced by regression of the hepatosplenomegaly, markedly reduced foamy macrophage infiltration in bone marrow, and STR-PCR of 90% (Short Tandem Repeat-polymerase chain reaction) at day 30. She has not had any serious problems except blood transfusion twice because of anemia, since transplantation 3 months ago. Her donor has shown symptoms of Multiple Sclerosis disease two months after transplantation. Follow-up will show the long term effect of BMT on her disease and neurocognitive development.

372

CHEDIAK-HIGASHI SYNDROME: COMPLETE ENGRAFTMENT AFTER DOCUMENTED CHIMERISM

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We describe a 7 year old male with a history of Chediak-Higashi syndrome who received a matched unrelated cord stem cell transplantation in the accelerated phase and achieved complete donor engraftment after initial partial chimerism. Chediak-Higashi syndrome is a rare autosomal disease characterized by partial oculocutaneous albinism, recurrent bacterial infections, mild bleeding diatheses, and both central and peripheral neuropathies. In late childhood, these patients develop an accelerated phase characterized by pancytopenia, hepatosplenomegaly, and lymphocytic infiltrates. Death associated with the accelerated phase is secondary to infection and hemorrhage. The diagnosis of Chediak-Higashi syndrome is made by microscopic visualization of the giant cytoplasmic granules in leukocytes or abnormal giant melanosomes in hair shafts. Curative treatment entails bone marrow transplantation. Hematopoietic chimeras have been documented with clinical improvement, particularly being free of the accelerated phase. Our patient demonstrated chimerism at 30 days post-transplantation. The DNA fingerprinting analysis at this time showed 30% donor and 70% recipient cells in the marrow. The neutrophils on the peripheral blood smear, which contained large purplish inclusion bodies, were far fewer than the number of normal neutrophils. At day 77, the peripheral smear showed normal neutrophils and no granulated leukocytes. Repeat bone marrow biopsy at 84 days post-transplant showed complete engraftment; 90% donor marrow. Although hematopoietic chimerism may result in significant clinical improvement of patients with Chediak-Higashi, there may be further self-selection for normal marrow cells over abnormal cells even after the initial engraftment of bone marrow transplantation.

373

UNRELATED DONOR UMBILICAL CORD BLOOD TRANSPLANTATION IN TWO CHILDREN WITH AMEGAKARYOCYTIC THROMBOCYTOPENIA WITH RADIO-ULNAR SYNOSTOSIS

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Congenital amegakaryocytic thrombocytopenia (CAMT) with proximal radio-ulnar synostosis is a rare autosomal dominant disorder of thrombopoiesis and forearm abnormality. Four children have previously been described in the literature, some with an identified mutation of the HoxA11 gene. The fathers of the previously reported children had skeletal abnormalities, however normal platelet counts. We describe 2 children from the same family who had radio-ulnar synostosis and CAMT and subsequently underwent unrelated donor umbilical cord blood transplant (UCBT). The mother has radio-ulnar synostosis without any hematologic findings. Both children lack HOXA11 mutations and demonstrated proximal radio-ulnar sysnostosis. The first child had thrombocytopenia at birth, with a bone marrow initially showing normal cellularity with significantly decreased megakaryocytes. She pro-